REMARKS

Upon entry of this preliminary amendment, claims 15-28 will be pending in this application. Claims 1-14 are sought to be (or have been) cancelled without prejudice thereto or disclaimer thereof the subject matter contained therein. Support for new claim 15 can be found, for example, in claims 1 and 13, in the specification at page 4, lines 1-4 and 20-31; and at page 7, lines 7-14. As described in the specification from page 6, line 27 to page 7, line 5, the Kyte-Doolittle hydrophobicity analysis is well known to the skilled artisan. Moreover, recitation of the term "combining" in claim 15 is meant to encompass the methods described in Applicants' specification at page 4, lines 25-31. These exemplary combining methods include

-- chemically, by coupling, conjugation or cross-linking, through dehydration, esterification, etc, of the amino acid sequences either directly or through an intermediate structure;
-- physically, by coupling through capture in or on a macromolecular structure; or
-- by molecular biological fusion, through the combination of recombinant nucleic acid molecules which comprise fragments of nucleic acid capable of encoding each of the two, such that a single continuous expression product is finally produced.

Support for new claims 16-28 can be found, for example, throughout the specification and in original claims 2-9, 13, 11, 12, 1 and 10 respectively. Applicant has also amended the specification to include a Cross Reference to Related Applications. Applicants respectfully assert that these amendments do not include new matter, and their entry is respectfully requested.

Response to Restriction Requirement

Applicants have cancelled all pending claims and presented new claims. It appears that the Restriction Requirement based upon alleged lack of unity was made between composition claims (Group I, claims 1-12) and method claims (Group II, claim 13). To the extent necessary, Applicants herewith elect Group II, and believe that new claims 15-28 are consonant with this election. If, however, the Examiner believes that some or all of claims 15-28 are not a part of

Group II, then Applicants request that the Examiner set forth another Restriction Requirement to which Applicants may respond.

Furthermore, and to the extent necessary, Applicants also elect Babesia, upon which claims 15-28 read.

Applicants make these elections ***with*** traverse. Further to 37 C.F.R. § 1.143, Applicants respectfully request that the Examiner consider the following remarks and reconsider and withdraw the Restriction Requirement.

Legal Standard for Determination of Whether Claims Have Unity of Invention

Because the captioned matter is a national stage application filed under 35 U.S.C. § 371, all claims possessing unity of invention must be examined together: "An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention")." 37 C.F.R. § 1.475(a) (*see also* M.P.E.P. 8th ed., rev. 4, § 1893.03(d) (2005): "Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371.")

The M.P.E.P. provides guidance as to when claims possess unity of invention:

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art.

M.P.E.P. 8th ed., rev. 4, § 1893.03(d) (2005). Hence, a genus claim comprising a special technical feature free of the prior art would possess unity of invention. Moreover, any dependant claims to sub-genuses or species falling within that genus would also be considered to possess unity of invention:

> If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any

> claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention. *Equally, no problem arises in the case of a genus/species situation where the genus claim avoids the prior art.*

M.P.E.P. 8th ed., Appendix AI, Annex B(c)(i) (2005, October revision) (emphasis added). Hence, all sub-genus or species claims that are dependent upon genus claims that possess unity of invention should be kept within the same group, as they also possess unity of invention.

Applicants' Special Technical Feature

Applicants' claim 15 is directed to a method of preparing an immunogenic composition comprising

i) combining a heterologous hydrophobic polypeptide to the N-terminus and/or the C-terminus of a core polypeptide thereby forming a fusion protein; and

ii) mixing said fusion protein with a saponin adjuvant in a free form, thereby forming said immunogenic composition;

wherein said heterologous hydrophobic polypeptide has a hydrophobicity of 0.6 or more as determined by dividing (a) by (b),

wherein (a) is the number of hydrophobic data points of said heterologous hydrophobic polypeptide as determined using the Kyte-Doolittle hydrophobicity analysis using a window of 5 amino acids, and (b) is the total number of amino acids of said heterologous hydrophobic polypeptide; and

wherein said core polypeptide has a protective epitope.

Applicants respectfully point out that the nature of the heterologous hydrophobic polypeptide is provided in the specification. In particular, Applicants' specification defines peptide hydrophobicity as follows:

> For the present invention, a peptide is considered hydrophobic if 60 % or more of the data points from the Kyte – Doolittle hydrophobicity analysis indicate a hydrophobic value; the hydrophobicity must be calculated using a window of 5 amino acids. The percentage

> hydrophobicity is calculated from the data table from such an analysis: the number of hydrophobic data points (the moving average numbers that are positive) is divided by the total number of aa of the peptide.

Specification, page 7, lines 7-12. Information about the Kyte-Doolittle (KD) hydrophobicity analysis is provided in the specification from page 6, line 27 to page 7, line 5.[1]

Hence, Applicants' claim 15 is a genus method claim with the following special technical feature: a method of making an immunogenic composition comprising a free saponin and a fusion protein, wherein the fusion protein comprises a heterologous hydrophobic polypeptide combined to the N-terminus and/or C-terminus of a core polypeptide having at least one protective epitope.

Reason for Traversal of Restriction Requirement

Applicants respectfully traverse the Restriction Requirement because the special technical feature of claim 15 is not anticipated or rendered obvious by the prior art.

The Examiner alleges in the Restriction Requirement that Gozar *et al., Experimental Parasitology* 97: 61-69 (2001) (herein, "Gozar *et al.*") "discloses an immunogenic composition that comprises a fusion protein and saponin adjuvant, wherein said fusion protein comprises a heterologous hydrophobic peptide which is fused to a core polypeptide which comprises at least one protective epitope . . . ." Restriction Requirement, page 3, lines 8-11. Applicants strongly disagree with this characterization of Gozar *et al.*

The fusion protein of Gozar *et al.* comprises Pfs25 and Pfs28, two peptides of *Plasmodium falciparum*. *See* Abstract of Gozar *et al.* Neither of these peptides are hydrophobic as defined by Applicants claim and specification. As described above, a peptide is hydrophobic only if 60 % or more of the data points from its Kyte – Doolittle hydrophobicity analysis indicate a hydrophobic value. Such an analysis performed over these peptides reveals that neither of them are hydrophobic. *See* Appendix A, provided herewith. Pfs25 has 217 amino acids, 100 of which

[1] Applicants note that the hydrophobicity percentages shown in Figure 1 are incorrect. The actual values are from top to bottom 81, 70, 81, 83 and 55%. Further explanation of this

have positive hydrophobicity scores. Hence, Pfs25 has a hydrophobicity of 100/217, or 46%. Pfs28 has 218 amino acids, 99 of which have positive hydrophobicity scores. Hence, Pfs28 has a hydrophobicity of 99/218, or 45%.

Hence, Gozar *et al.* does not describe the special technical feature of Applicant's genus claim 15. Accordingly, claim 15 and all of its dependent claims possess unity of invention and restriction of that claim or its dependent claims to a particular sub-genus or species is improper. Thus, claim 15 and all of its dependant claims possess unity of invention and should be examined together.

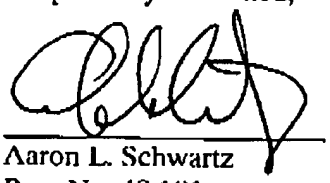
unintentional error and correction of Figure 1 will follow.

Conclusion

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Applicants submit that this application is in condition for allowance, and request that it be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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Attorney Docket: I-2002.010 US

EXHIBIT A

Pfs25 (Genbank: P13829)

mnklysiflffiqlsikynnakvtvdtvckrgfliqmsghleckcendlvlvneetcee
kvlkcdektvnkpcgdfskcikidgnpvsyackcnlgydmvnnvcipnecknvtcgngkc
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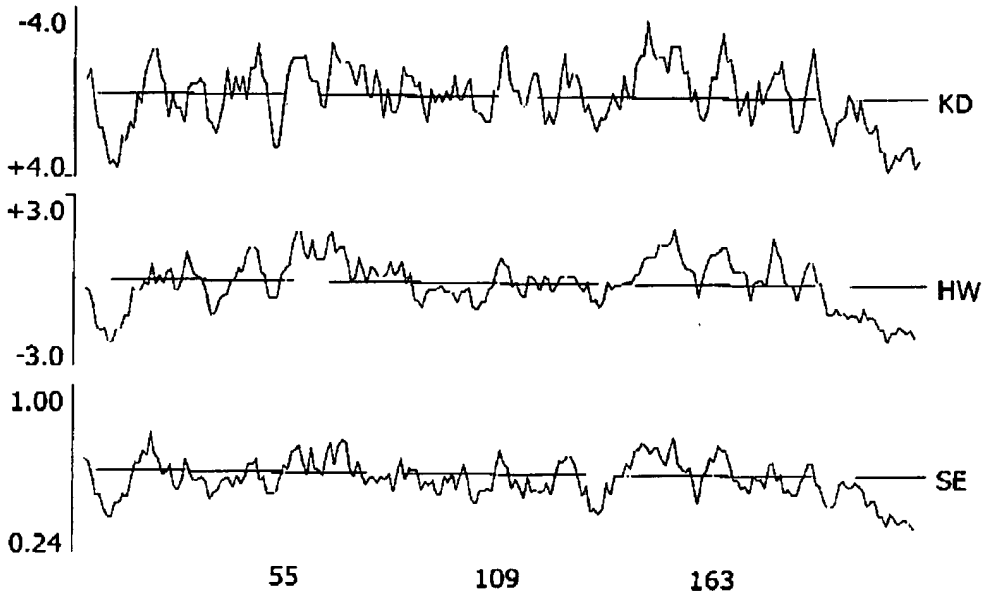

Pfs28 (Genbank: AAT00624)

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kvvcdkvensfkacdeyaycfdlgnknnekqikcmcrteytltagvcvpnvcrdkvcgkg
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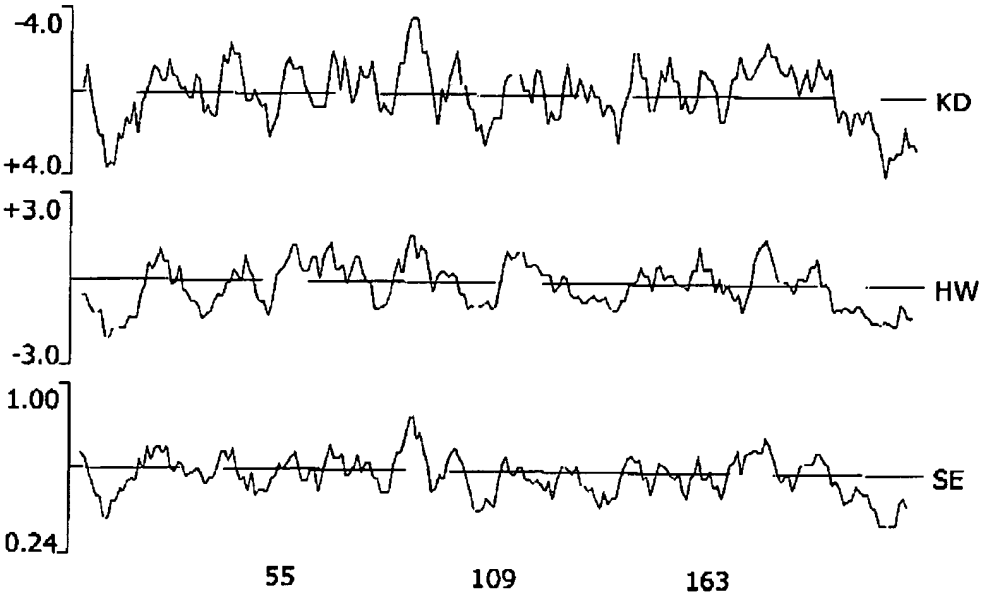

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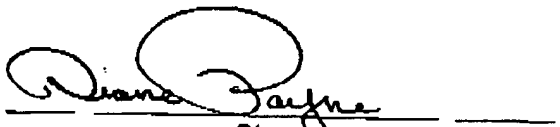

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USSN: 10/520,698
Application of: Gorenflot, *et al.*
For: Immunogenic Composition
Attorney Docket: I-2002.010 US

Preliminary Amendment and Response to Restriction Requirement of 4/27/06 (11 pages)
Exhibit A (3 pages)
Facsimile Coversheet (1 page)
Certificate of Facsimile Transmission (1 page)